



MAIL STOP - PCT
Docket No. 27528U

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor: MENGE, et al. Art Unit: XX
Appl. No.: 10/587,836 Examiner: XX
Filing Date: July 28, 2006 Confirm. No.: XX
Intl. Appl. No.: PCT/EP2005/050415
Intl. Filing Date: February 1, 2005
Title: 2-(PIPERIDIN-4-YL)-4,5-DIHYDRO-2H-PYRIDAZIN-3-ONE DERIVATIVES
AS PDE4 INHIBITORS

TRANSMITTAL LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

Submitted herewith for filing in the U.S. Patent and Trademark Office is the following:

1. Submission of Documents to Supplement Filing Documents under 35 USC 371;
2. PCT/IB/373 (International Preliminary Report on Patentability); and
3. PCT/ISA/237 (Written Opinion of the International Searching Authority).

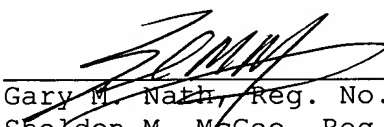
The Commissioner is hereby authorized to charge any deficiency or credit any excess to Deposit Account Number 14-0112.

Respectfully submitted,

THE NATH LAW GROUP

January 29, 2007

THE NATH LAW GROUP
112 South West Street
Alexandria, VA 22314


Gary M. Nath, Reg. No. 26,965
Sheldon M. McGee, Reg. No. 50,454
Customer No. 34375

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SUBMISSION OF DOCUMENTS TO SUPPLEMENT FILING DOCUMENTS
UNDER 35 USC 371

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In order to supplement the filing documents for the national phase filing Under USC 371 commenced on July 28, 2006, applicant now submits the following documents:


1. PCT/IB/373 (International Preliminary Report on Patentability); and
2. PCT/ISA/237 (Written Opinion of the International Searching Authority).

Please charge any deficiency or credit any overpayment to our Deposit Account Number 14-0112.

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 1240WOORD01	FOR FURTHER ACTION		See item 4 below
International application No. PCT/EP2005/050415	International filing date (<i>day/month/year</i>) 01 February 2005 (01.02.2005)	Priority date (<i>day/month/year</i>) 04 February 2004 (04.02.2004)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant ALTANA PHARMA AG			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | |
|--|---|
| <input checked="" type="checkbox"/> Box No. I | Basis of the report |
| <input checked="" type="checkbox"/> Box No. II | Priority |
| <input checked="" type="checkbox"/> Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> Box No. VI | Certain documents cited |
| <input type="checkbox"/> Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Date of issuance of this report 07 August 2006 (07.08.2006)
	Authorized officer Ellen Moyse e-mail: pt05@wipo.int

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 30 JUN 2005

PCT

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To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2005/050415

International filing date (day/month/year)
01.02.2005

Priority date (day/month/year)
04.02.2004

International Patent Classification (IPC) or both national classification and IPC
C07D401/04, C07D401/14, A61K31/497, A61P11/00

Applicant
ALTANA PHARMA AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80293 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
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Authorized Officer:

Weisbrod, T

Telephone No. +49 89 2399-8931



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/050415

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☐ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:
see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/050415

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 17, 18

because:

☒ the said international application, or the said claims Nos. 17, 18 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/050415

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-18
	No: Claims	
Inventive step (IS)	Yes: Claims	1-18
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-16
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10).

and /or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2005/050415

Re Item I

Basis of the opinion

The application is directed to

- (i) 2-(piperidin-4-yl)-pyridazin-3-ones (1) (claims 1-13),
- (ii) the medical use of compounds (1) (claim 14),
- (iii) a pharmaceutical composition comprising a compound (1) (claim 15),
- (iv) the second medical use of compounds (1) (claim 16), and
- (v) the corresponding therapeutic methods (claims 17-18).

Re Item II

Priority

The claimed date of priority does not appear valid for compounds (I) wherein R^{22} and R^{23} together form ring systems selected from morpholin-3,5-dione-4-yl to isoindol-1,3-dione-2-yl according to claim 1, the claims 2-13, and subject matter referring to these compounds respectively claims.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 17 and 18 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1 Reference is made to the following documents.

D1: EP-A-0 738 715, 23.10.1996; cited in the application.

D2: WO 02/064584 A, 22.08.2002; cited in the application.

D3: WO 02/085906 A, 3110.2002; cited in the application.

D4: WO 2004/018449 A, 04.03.2004.

D4 was published after the priority date. Under the presumption that the priority is valid for the claimed matter the said document is not considered as prior art under Rule 64.1 PCT.

2 Novelty

2.1 **D1** relates to pyridazinone derivatives as PDE4 inhibitors. The present compounds (1) differ from the compounds of **D1** through the 1-R⁹-piperidin-4-yl group and in having the R¹/R² alkyl groups in position 4 rather than in position 5. The present claimed matter is thus novel vis-à-vis **D1**.

D2 and **D3** relate to phthalazinone derivatives as PDE4 inhibitors. The present compounds (1) differ from the compounds of **D2/D3** insofar as they represent monocyclic pyridazinones rather than bicyclic phthalazinones. The present claimed matter is thus novel vis-à-vis **D2/D3**.

2.2 The P-document **D4** relates also to phthalazinones as PDE4 inhibitors, whereas the application is directed to pyridazones. **D4** will, thus, not become relevant to the question of novelty of the application.

4 Inventive Step

4.1 The application describes the preparation of certain compounds (1) and shows that such compounds exhibit PDE4 inhibitory activity (the application, page 34).

4.2 In view of **D1** as most relevant state of the art the problem underlying the application may be seen in the provision of further PDE4 inhibitors. The present compounds (1) differ from those of **D1** in bearing in the 2-position a 1-R⁹-piperidin-4-yl substituent rather than a group -Q-R⁵ and in bearing the two R¹/R² alkyl substituents in position 4 instead of 5. Although the documents **D2** and **D3** teach already that the present R⁹-piperidin-4-yl substituents are compatible with the desired activity, it does not appear